Case Reports

Congenital acinar dysplasia

Familial cause of a fatal respiratory failure in a neonate

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ABSTRACT

Pulmonary hypoplasia is a rare cause of pulmonary insufficiency, and has a significant rate of morbidity and mortality among affected infants. In most cases, pulmonary hypoplasia is secondary to underlying abnormalities. These may include space occupying lesions, as in infants with congenital diaphragmatic hernia; malformation of chest wall resulting in a small thoracic cavity; severe and prolonged oligohydramnios; and neuromuscular disorders, which prevent normal fetal chest expansion. All lead to poor lung development. Primary pulmonary hypoplasia as a result of congenital acinar dysplasia is exceedingly rare and is diagnosed by exclusion of all known etiologies of secondary pulmonary hypoplasia.

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Congenital acinar dysplasia (CAD) has been diagnosed and reported in a few cases in the literature.[1-4] In those 5 reported cases, the newborn had survived for only a short time and autopsy (of the normal appearing infants) revealed hypoplastic lungs with major bronchial-tree development but no acinar development. In CAD, the acini (the respiratory bronchioles, alveolar ductus, and alveoli) fail to develop. The lungs at term will have the appearance of the pseudoglandular phase of 16 weeks gestation.[3] To heighten awareness of this rare form of respiratory failure and to include it in the differential diagnosis of primary respiratory failure, we report on a family with one proven case and 2 suspected isolated congenital acinar dysplasia.

Case Report. A female infant was born at 37 weeks gestation to a 33-year-old Saudi mother, gravida 12 para 10 and one abortion. Antenatal ultrasound (US) examination in the 32nd week of gestation showed mild oligohydramnios with no congenital malformations. There was no history of premature rupture of membrane or intrapartum fetal distress. The mother had one abortion, one intrauterine fetal death, and 2 infantile deaths. The remaining siblings are alive and well. Of the 2 infantile deaths, the first infant was a female, product of a full-term normal delivery, which developed severe respiratory failure of unknown etiology shortly after birth, and died at 2 months of age. The 2nd infant, also a female, developed severe respiratory failure soon after birth and died at 75 days on mechanical ventilator. Both were treated in a peripheral hospital and the lung biopsy was not obtained. The parents are healthy and not related. This infant was born vaginally with Apgar scores of 7, 9 and 10 at the first, 5th and 10th minutes. Immediately after delivery, the infant appeared normal and established spontaneous breathing. The weight of

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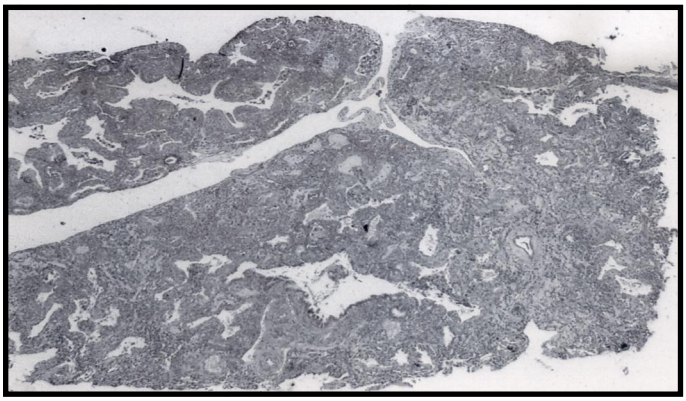

Figure 1 - Low power micrograph shows immature lung parenchyma composed of scattered airways, immature airspaces and intervening connective tissue.

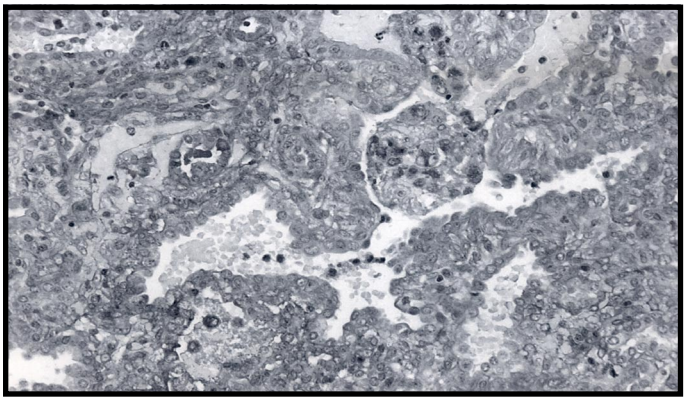

Figure 2 - High power micrograph shows immature lung tissue parenchyma with acini lined by cuboidal epithelium and blood vessels closely related to airspaces suggestive of sacular phase of development.

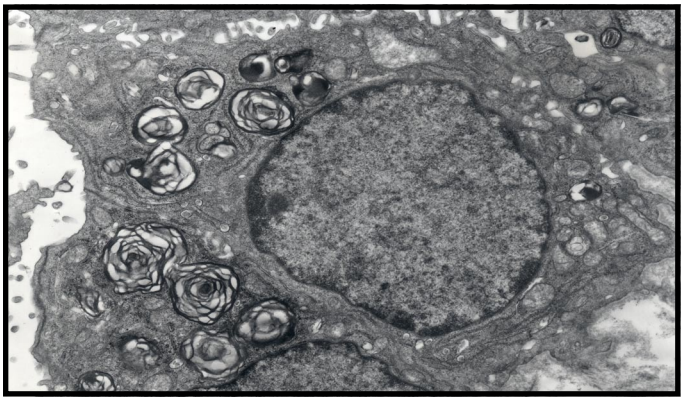

Figure 3 - Electromicrograph showing type II pneumocyte with abundant surfactant bodies.

the infant was 2.4 kg (25%), the length was 41 cm (10%) and the head circumference was 30 cm (10%). At 6 hours of age, the infant developed progressively severe respiratory distress with hypoxemia and hypercapnia, which required intubation and mechanical ventilation. The chest x-ray showed reduced lung volume and increased pulmonary vascularity. The infant had normal renal US. Gradually, the condition of the infant worsened that requires a higher ventilator settings. To reduce lung barotrauma and to improve oxygenation, she was shifted to high frequency oscillatory ventilator (HFOV). A trial of 3 doses of natural surfactant was given at the 2nd day of life, producing only a transient and minimal response. The infant did not tolerate trials of weaning from mechanical ventilation, and each time showed deterioration despite the administration of steroids to facilitate weaning. At the age of 2 months, a lung biopsy was performed. Microscopically, the lung biopsy showed pulmonary hypoplasia with arrest of lung growth at the acinar stage **(Figures 1 & 2)**, and the electron microscopy showed plenty of lamellar bodies in type II peumocytes **(Figure 3).** The lung biopsy findings and their implications were explained to the family. The fact that there was no alternative treatment available to this infant, it was discussed fully with the family and the decision was made to withdraw HFOV and shift the infant to conventional ventilation. Shortly thereafter, at the age of 3 months, the infant expired.

Discussion. A classic description of fetal lung development has generally included the embryonic, pseudoglandular, canalicular, sacular and alveolar phases.[5] The embryonic phase is characterized by the formation of lung budding during the first 7 weeks of intrauterine life. During the pseudoglandular phase, which occurs between the 8th and 16th week of gestation, there will be rapid proliferation of the primitive airways so that all airway divisions are more or less completed by 16 weeks. In the canalicular phase, occurring between the 17th and 27th weeks, the acinar structure of the lung is formed by air spaces appearing as saccular structures, and by vascularization of the mesenchyme during the saccular phase, which started after the 28th week of gestation. The saccular walls are narrow. The interstitial tissue decrease and distal air spaces are subdivided, producing terminal sac phase. The alveolarization stage begins from the 36th weeks through infancy, but can begin as early as 32 weeks.[5] To date, only a limited number of cases of primary pulmonary hypoplasia have been reported in the literature, with both sporadic[6,7] and familial occurrence.[8,9] All of these cases have different uniformity in the histopathology. Although our patient had prolonged ventilation before the lung biopsy, which might have changed the lung pathology, all efforts were made to reduce the lung damage, including the use of HFOV and the acceptance of low normal Pao2. The histopathology of barotrauma and oxygen toxicity was

not seen in this patient's lung. The pulmonary histopathology of our patient suggests that the lungs were developed through the pseudoglandular stage, but the canalicular phase was dysplastic. The etiology and pathology of the pulmonary acinar dysplasia are not well known, although it was postulated that it may be an intrinsic defect of the lung mesoderm. This rare form of severe primary pulmonary hypoplasia differs from other causes of respiratory failure, such as surfactant-protein B deficiency (SP-B deficiency). Both develop primary, severe respiratory failure, but the lamellar bodies are absent in patient with SP-B deficiency, while they are present in the CAD-patient.[10] The presence of dysplastic lung tissue on histopathology and lamellar bodies in EM support the diagnosis of CAD and make the diagnosis of SP-B deficiency unlikely. Meorman et al[4] had reported for the first time a family with 2 female infants having severe primary pulmonary hypoplasia, diagnosed as congenital acinar dysplasia. He suggested the presence of an autosomal recessive mode of inheritance for a gene critical for normal lung parenchymal development. We believe that our case (with the family history) is highly suggestive of an inherited disease. As well, all reported cases are females[1-4] this may raise the possibility of X-linked dominant type of inheritance.

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